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Title	**Variability of waiting times for the four most prevalent cancer types in Ontario: a retrospective population-based analysis**
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Reviewer 1	Dr. Robert Anton Olson
Institution	BC Cancer Agency, Centre for the North, Radiation Oncology, Vancouver, British Columbia
General comments (author response in bold)	This is a simple, well written study. This data will be important for administrators, researchers, and clinicians. **We thank the reviewer for the positive comments.** As an oncologist from outside of ON, I have a vague understanding that changes in billing may have had an impact on the number of patients radiation oncologists see, and therefore the wait times. However, this retrospective study does not discuss this potential cause or others in sufficient detail. **There may have been changes in the fee schedule over this time period. It is beyond the scope of this study to relate these changes to changes in waiting time. However, we suspect that other system level changes (for example, Cancer Care Ontario's policies on providing more equitable services) were more also important.** 1. I think this manuscript could be improved by a more fulsome discussion of some of the changes that occurred during or before this era that may have resulted in some of the changes. **In the current version, we have enhanced our discussion of potential efforts that might have caused changes over time. We mention that Cancer Care Ontario has had consistent policies over past years to provide the same level of service for Ontarians regardless of their geographical location and demographic characteristics. These policies, for example, could have been a main driver for changes that we report in this paper.**
Reviewer 2	**Mrs. Jina Zhang-Salomons**
Institution	Queen's University Cancer Research Institute, Kingston, ON
General comments (author response in bold)	This is a large population-based study reporting the temporal trend in waiting times for major types of cancer treatments during the recent decade. The report is well-written. Some suggestions to strengthen the study: Major points: 1. In literature, time to cancer treatment has been frequently described by 2-time intervals: time from symptom onset to diagnosis (diagnosis interval) and time from diagnosis to treatment (waiting for treatment). Diagnosis interval concerns health services in primary care, and waiting for treatment concerns specialized care in large institutions. The current study used "care seeking date" as a proxy for the symptom onset date and investigated the overall time from care seeking to treatment. Your data provide opportunity to divide up this time span into diagnosis interval and waiting for treatment. Such sub-analyses would be informative to patients as well as care providers, and also can help better isolate the effect of changes in treatment patterns on your results. **As suggested by previous research, it is the perceived waiting time (the period from symptom onset to the start of treatment) that plays a key role in a patient's satisfaction from the care service provided to the patient.[4] However, most of waiting time related studies only focus on parts of the perceived waiting time, namely (1) family physician referral to a specialist visit, and (2) diagnosis to treatment. In this study we do not focus on these components because our main interest in this paper is to analyze perceived waiting time using administrative data to address shortcomings of present studies that are mainly based on surveys, and therefore have small sample sizes.** 2. The majority of the previous studies cited from literature concern the psychological effect of delay in diagnosis. Please also include references on the effect of delay in treatment (from diagnosis) on survival outcome. **We added the sentence below to the Introduction section to quantify the negative impact of a delayed treatment on prognosis and treatment outcome.** **" In a UK research study conducted on a group of prostate cancer patients, extended treatment waiting times led to growth in cross-sectional tumor size up to 373% and 21% of the patients became medically incurable. "** 3. For the regression analysis, please comment on what you observed in residual analysis. Were the assumptions of normality and equal variance met? If not, what method did you use to test the significance of the slopes? **We used probability plots with a 95% confidence interval to check the normality assumption of residuals and used residuals vs. fitted plots to check the assumption of constant variance. We did not observe any systematic deviation from normality assumptions, especially at tails. We present the plots and a detailed discussion of results in the Appendix section.** 4. It is unusual to use CV as a response variable in a simple linear regression, since CV often has a skewed distribution. If the distribution is indeed skewed, there are different models to handle it (e.g. regression on log CV). Please comment. **We compared the performance of our linear models with log-linear models. The probability plots and residuals vs. fitted plots were very similar to those shown in Figures 1R-4R. We preferred to stay with our linear models since coefficients of a log-linear model do not have as clear interpretations as in a linear model.** Minor point: 5. Page 4 line 34: please provide a reference for the "98%".

	We have added a reference.
Reviewer 3	**Tiffany Rose Haig**
Institution	Alberta Health Services, Cancer Control, Calgary, Alta.
General comments (author response in bold)	Thank you for the opportunity to review the excellent paper entitled, "Waiting Times for the Four Most Prevalent Cancer Types in Ontario". The aim of the paper, as stated by the authors, was to examine the quality of service that patients diagnosed with the four most prevalent cancer received in the province of Ontario, Canada from 2002 to 2012. The authors evaluated wait times by studying trends in both the median and the coefficient of variation (CV) of waiting times. This research should be of interest to Canadian audiences. Overall, it was a pleasure to read this well-written and informative paper. The authors did an excellent job at detailing the burden of cancer on the Canadian population and the importance of quantifying treatment wait times. There were a few comments and suggestions noted below which may improve the paper. 1. One of the major concerns I have with this paper is that the authors do not adjust/or account for lack of adjustment, for sociodemographic factors including age, sex or geographic location which affect access to care, referral and treatment wait times. **We agree that sociodemographic factors like age, gender or geographic location (rural vs. urban) may have significant impacts on waiting times *at the individual level*. However, all of our regression analyses are at the aggregate level, i.e., each data point represents all patients with that type of cancer that year. It is not clear that adjusting for these factors at the aggregate level would be beneficial. Thus, we limited our analyses to simple linear regressions, stratified by cancer and treatment type, using time as the only independent variable. We have included some text in the discussion section to comment on this point.** Title 2. The authors should consider specifying the study design type to make their title more informative. **The title has been changed.** Abstract 3. If possible include details of statistical methodology, specifically CV since it is an important feature of this work. **In the abstract, we now mention that we use regression analysis to identify the trends in the median, CV, and Gini coefficient of the waiting time.** Section 1. Introduction 4. Page 3, Lines 21-40: Could you please add some details to this section quantifying the burden of wait times on cancer-specific mortality, progression, even recurrence or even patient distress? **We added the sentence below to the Introduction section to quantify the negative impact of a delayed treatment on prognosis and treatment outcome.** **"In a UK research study conducted on a group of prostate cancer patients, extended treatment waiting times led to growth in cross-sectional tumor size up to 373% and 21% of the patients became medically incurable."** 5. Page 3-4, Lines 43- 6: Additionally, could you please state whether or not the CV method has been used in this capacity previously or in any type of health-related research? **To the best of our knowledge, although it is very common in healthcare-related papers in the field of Business Analytics to use CV in waiting time analyses (e.g., 1R), we have not seen the CV to be used in health-related journals. Using the Coefficient of Variation in this paper provides us with an opportunity to use this measure in public health and health policy literature, in which this measure has been overlooked while it can be very useful in contexts like waiting time analysis. As suggested by the editorial team, we repeated our analyses with a more popular measure in the health care field, the Gini coefficient, which supported our original findings. We have added our Gini coefficient results to the paper, along with a new figure (Figure 4) that illustrates the trend for all cancer type-treatment type pairs, and additional content in Table 2 where we now report slopes for both the CV and the Gini coefficient. We have also added a paragraph to the discussion about this point. We feel that this strengthens the study as there are now two measures that point to the same conclusion – that waiting times became more consistent over the study period.** 6. Other: The contribution that this paper intends to make, beyond the aim to quantify wait times within incident cancer cases, is unclear. Could the authors could clearly state the novel/main contribution of this paper to the existing body of literature? **We have updated the Strengths and Limitation section to make our contributions, and also limitations of the paper, clearer. In short, our contributions are:** **1) Providing and approximation for patient perceived waiting time that allows us to use administrative data with large sample sizes to analyze the waiting times whereas previous work was based on surveys, and therefore had small sample sizes.** **2) We introduce the CV as a measure of cancer care equity.** Section 2. Methods 7. 2.1 Data Sources – Please include a quality assessment of the Ontario Cancer Registry (OCR), while the authors suggest it contains detail of 98% of incident malignancies, what is the quality of the data? Please also make a similar statement for the Ontario Health Insurance Plan (OHIP) since it is based on physician billing. **Due to word count limitation, we could not discuss the quality of these datasets in the paper. However, we added references that discuss these topics.**

8. 2.2 Variable Definitions and Main Outcome Measure – Please list out examples of terms for "potentially-diagnostic procedures" and "diagnostic outcomes" or give definitions for both as a quality assessment indicator. Please indicate how many individuals were tasked with identifying these pieces of information, was there any verification practices done or rater agreement?

In the current paper, we have added examples where we define the variables to make them clearer. Recognizing the risk of misclassification bias in the context of an administrative healthcare dataset, potential diagnostic procedures and outcomes, in accordance with cancer care Ontario clinical pathway management guidelines, were classified by a single investigator, with potential discrepancies brought forward to obtain consensus within the broader research group.

9. 2.3 Statistical Analyses – The authors modelled the median wait time between diagnosis and first treatment using linear regression but only considered treatment type as predictors in the model and then stratified by cancer type. Were the authors able to control for any potential confounders/sources of variability in their models such as age, gender or geographic location (rural vs. urban)? All of which have been shown to affect access to care, quality, and care-related services? It is well known that access to primary care services and subsequent treatment opportunities are affected by these factors. The reviewer suggests that the authors either adjust their models for these factors, if possible, or at the least mention this as a notable limitation of the study.

As noted in previous responses, sociodemographic factors like age, gender or geographic location (rural vs. urban) may have significant impacts on waiting times *at the individual level* and, in the case of "rural vs. urban", at the sub-group level. However, all of our regression analyses are at the aggregate/provincial level, i.e., each data point represents all patients with that type of cancer that year. It is not clear that adjusting for these factors at the aggregate level would be beneficial. Thus, we limited our analyses to simple linear regressions, stratified by cancer and treatment type, using time as the only independent variable. We have included some text in the discussion section to comment on this point.

Section 3. Results
10. Page 5, line 57: how do the proportions of cancer types observed compare to those of the general population? Please discuss in the discussion section.

Our cohort was derived from data in the Ontario Cancer Registry, which is considered to be >98% accurate. However, to validate, we compared our numbers with a Statistics Canada report on the distribution of cancer incidence in Canada in 2007 (the middle of our study period).[3R] Our sample contains 24% lung cancer, 26% breast cancer, 27% prostate cancer, and 23% colorectal cancer. The Statistics Canada report shows, among the four cancer types included in our study, 26% lung cancer, 24% breast cancer, 26% prostate cancer, and 23% colorectal cancer, which is approximately in line with our sample.

11. Other: see note above under "statistical analyses" sub-heading. The authors did not account for any sociodemographic factors (e.g. location, age, and sex). Can the authors please indicate whether any literature shows evidence of sociodemographic factors influencing cancer care wait times? I was under the impression that geographic location may be a significant predictor of access to care services (primary physicians) and subsequent referrals and treatment opportunities. Ontario is noted to have a significant rural population.
Prior research demonstrates the importance of these factors at the individual level.[2R] However as noted in our responses above, our regression analyses are all at the aggregate level (i.e., each data point represents all cases of that type for the year) and it is not clear how we would adjust for the proportion of the population having a given characteristic. Thus, we have continued to use regression models where time is the only covariate.

12. How are these results possibly affected by rising rates of some cancers (breast cancer) but leveling rates of other cancers (lung cancer)?

The importance of studying wait times also needs to be considered in the context of the changing rates of some cancers, due to public health initiatives (i.e. population-wide screening programs) and changes in the exposure pattern of risk factors (i.e. smoking). As an example, CT-screening for individuals at increased risk of lung cancer may result in an increased incidence of lung cancer observed in the upcoming years in the province of Ontario. This may result in an increase in waiting times observed. In the current version of the paper, we mention this in the Interpretation section.

Section 4. Interpretation
13. Page 7, line 14-43: Please recommend future directions related to this topic or more specifically how the hypothesis proposed by the authors may be scientifically tested. Is it also possible that screening services are improving leading to fewer check-ins prior to referral to specialist? It may also be of interest if the authors hypothesize for inconsistency across wait time results. Please suggest potential sources of variability in these findings.

Different cancer types may different characteristics, different rising rates, for example, as discussed in our response to the previous comment (Comment 12). Unless we have appropriate data that we could thoroughly investigate causalities, any comment on why waiting times for different cancer types have evolved differently would only be a speculation. In the current version, we mention this potential differences in cancer characteristics but we do not comment on causalities.

14. Page 7: Please consider discussing/hypothesizing how the quality of service may have continued to changed from 2012 to present day.

All changes and improvements in cancer care that we report in this paper are results of policy improvements and technological advancements. We do not have any reasons to believe those policy and technological improvements stopped in 2012. Therefore, we expect that improvements reported in this paper continued to get better after 2012 as well (i.e., continued improvements in consistency of waiting times). Some of those continuous policy improvements in cancer care has been reported in Ontario Cancer Plan IV (Paper 2).

15. Page 7-8, lines 46-8: The authors should consider spending a little bit more time comparing

and contrasting findings with other national, provincial or international cohort studies. How are these finding applicable to other universal healthcare systems?

We agree with the suggestion as a priority area of research. These comparative suggestions will be the subject of future research within our group. In the current paper, we briefly compare our results with other papers in the literature where we mention references 23, 24, and 25.

16. Page 9, Line 6: correct grammatical error, "small sample size"
In the new version, that sentence does not exist.

17. Other: As per Figure 3 (The coefficient of variation of waiting times) please discuss why such discrepancies may exist for between surgery type and wait times for some cancers (Colorectal Cancer) but not others (Lung Cancer). There appears to be a convergence of wait times across all treatment types overtime, what other factors may explain this?

The purpose of the study was to identify variation and changes in variation over time, both of which can be informative for the relative policy maker within that area of management. We did not study causality, but speculate that system level changes in processes may have contributed. Proving this hypothesis is beyond the scope of the current study.

Section 5. Strengths and Limitations
18. As suggested above under sub-heading "statistical analyses" if the authors are unable to control/adjust for geographic location this should be noted as a limitation of the study given that ~20% (or 2.6 million) Ontario residents are considered rural.

We list as one of limitations of this work that "we could not include sociodemographic and socioeconomic factors in analysis due to the lack of these data [in our datasets]."

19. Other: Further limitations include the inability to generalize the findings further than the province of Ontario.

It is added as one of limitations of this work.

20. I think there are a number of other important limitations that the authors may consider mentioning including:
- No way to assess reasons for delays between care seeking date and first treatment date. What does the literature suggest are reasons delays occur?

The updated Strengths and Limitation section includes all limitations discussed in the review document including the lack of data about delay reasons.

21. Why did the authors choose not to include an "other" treatment group, it appears that a significant "other group" may have been important especially for lung cancer or other drug treatments.
- What about the inability to assess and factor in cancer stage? You would expect wait times to be significantly lower for those with more progressed or aggressive cancer types. Please explain sources of variability.

We did not include an "other" group because that would include different cancer types that are managed completely differently, in terms of both diagnosis and treatment. Therefore, we decided to focus on the main 4 cancer types with the largest health impact. The other cancers would be of consideration for individual analyses in the future, but not lumped together, by our group. We provide a detailed discussion about our rationale for focusing on the main 4 cancer types in our response for the first comment of Senior Editor.

22. What about the strengths of the study? Are the authors able to make a statement as to the contribution that this paper makes?

We have updated the Strengths and Limitations section.

Section 6. Conclusions
23. Page 9, line 55: Please be sure to indicate applicable location i.e. Ontario in your concluding remarks, "…for all cancer types between 2002 and 2012 in the province of Ontario, Canada".

We added the location.